Introduction The Burden of Bipolar Depression

Charles L. Bowden, M.D., Guest Editor

ipolar disorder is a common, debilitating illness that is associated with significant morbidity and mortality.1 Depression is the predominant mood symptom expressed in patients with bipolar disorder, with most patients having clinically significant depressive symptoms about 3 times longer than manic symptoms.^{2,3} Despite this, bipolar depression is often underrecognized or misdiagnosed as major depressive disorder (unipolar depression). Misdiagnosis may be due to similarity of symptoms and the occurrence of comorbidity, such as alcohol or substance dependence.⁴ Clinicians must be aware of the symptomatic presentation of patients with bipolar depression, as this phase of the illness accounts for most of the morbidity and mortality of the disorder. For example, depression in patients with bipolar disorder has been associated with poorer life functioning.⁵ Another major concern with this phase of the illness is the increased risk of suicide, with up to 20% of patients with bipolar disorder completing the act.6,7

The impact and treatment challenges presented by bipolar depression, and future approaches to addressing these issues, were discussed at an AstraZeneca-sponsored roundtable meeting held in New York, N.Y., in April 2004. The outcome of those discussions and a review of the possible mechanisms of action underlying the efficacy of atypical antipsychotics in bipolar depression are presented here.

In the first article of this supplement, Robert M. Post, M.D., who works in private practice and is head of the Bipolar Collaborative Network in Chevy Chase, Md., reviews the substantial impact of bipolar depression on patients with bipolar disorder, their families, and caregivers. In comparison to unipolar (i.e., major) depression, bipolar depression may result in a greater overall burden on patients and families due to an earlier age at onset, more frequent episodes, and a greater proportion of time spent ill.⁴ Bipolar disorder overall also results in direct and indirect financial costs, including inpatient and outpatient care and lost work days. Dr. Post emphasizes the need for early, accurate diagnosis of the illness and particularly of bipolar depression.

Trisha Suppes, M.D., Ph.D., and colleagues from the University of Texas Southwestern Medical Center in Dallas then review the challenges that clinicians face with bipolar depression, including diagnosis and management. The need for adequate history-taking to accurately distinguish bipolar illness from unipolar depression or other illnesses and the optimization of treatment are emphasized. The key challenges that remain to be addressed are early, appropriate diagnosis; the identification of patients most likely to benefit from treatment; the most appropriate treatment options; the identification of specific symptoms that may be improved with treatment; and the definition of the long-term treatment needs of patients with bipolar depression. The differences between subtypes of bipolar disorder and any symptomatic and/or treatment differences between men and women also warrant further study.

Heinz Grunze, M.D., Ph.D., from the Ludwig-Maximilians University in Munich, Germany, begins reviewing the therapeutic options for bipolar depression in the next article. He presents the current evidence for the use of lithium, anticonvulsants, and traditional antidepressants for the treatment of bipolar depression. He focuses on the use of traditional antidepressants, which are generally not recommended as monotherapy due to the associated risk of switching patients into mania. However, Dr. Grunze also presents the reasons and circumstances in which traditional antidepressants such as the selective serotonin reuptake inhibitors may be warranted.

The use of atypical antipsychotics in bipolar depression is discussed by Joseph R. Calabrese, M.D., and colleagues from the University Hospitals of Cleveland/Case Western Reserve University School of Medicine in Cleveland, Ohio. This article reviews the randomized, controlled clin-

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ical trials of olanzapine monotherapy, olanzapine in combination with fluoxetine, and quetiapine monotherapy that provide evidence for the efficacy of these medications in patients with bipolar depression.

The next article, by Eduard Vieta, M.D., Ph.D., from the Hospital Clinic, University of Barcelona in Barcelona, Spain, reviews the benefits of psychosocial interventions in addition to pharmacotherapy in the treatment of bipolar depression. Dr. Vieta discusses recent data that suggest that the use of long-term psychosocial interventions in such patients may decrease the risk of relapse, improve patient adherence to treatment regimens, and decrease the number and length of hospitalizations.

Lakshmi N. Yatham, M.B.B.S., F.R.C.P.C., M.R.C. Psych., from the University of British Columbia in Vancouver, B.C., and colleagues complete the discussion on bipolar depression by presenting the mechanisms of action of atypical antipsychotics, namely olanzapine and quetiapine, that may underlie their efficacy in this phase of the illness and contrasting those mechanisms with the known mechanisms of action of traditional antidepressants.

This supplement highlights the impact of bipolar depression, describes the challenges that clinicians still face in the optimal diagnosis and treatment of this phase of bipolar disorder, and offers an insight into the mechanism by which agents that have proven efficacy may be working in bipolar disorder. It is hoped that these articles will induce further thinking and research in this area, as early and accurate diagnosis, aggressive management, and early, effective therapy are needed to overcome the impact of depressive episodes in patients with bipolar disorder.

REFERENCES

- Post RM, Denicoff KD, Leverich GS, et al. Morbidity in 258 bipolar outpatients followed for 1 year with daily prospective ratings on the NIMH Life Chart Methods. J Clin Psychiatry 2003;64:680–690
- Judd LL, Akiskal HS, Schettler PJ, et al. The long-term natural history of the weekly symptomatic status of bipolar I disorder. Arch Gen Psychiatry 2002;59:530–537
- Judd LL, Akiskal HS, Schettler PJ, et al. A prospective investigation of the natural history of the long-term weekly symptomatic status of bipolar II disorder. Arch Gen Psychiatry 2003;60:261–269
- Bowden CL. Strategies to reduce misdiagnosis of bipolar depression. Psychiatr Serv 2001;52:51–55
- Morris CD, Miklowitz DJ, Wisniewski SR, et al. Care satisfaction, hope, and life functioning among adults with bipolar disorder: data from the first 1000 participants in the Systematic Treatment Enhancement Program. Compr Psychiatry 2005;46:98–104
- Goodwin FK, Jamison KR. Manic-Depressive Illness. New York, NY: Oxford University Press; 1990
- Leverich GS, Altshuler LL, Frye MA, et al. Factors associated with suicide attempts in 648 patients with bipolar disorder in the Stanley Foundation Bipolar Network. J Clin Psychiatry 2003;64:506–515